UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,120	01/12/2001	Sarah S. Bacus	MBHB01-033	1979

20306 7590 12/13/2002

MCDONNELL BOEHNEN HULBERT & BERGHOFF
300 SOUTH WACKER DRIVE
SUITE 3200
CHICAGO, IL 60606

EXAMINER
GABEL, GAILENE

ART UNIT	PAPER NUMBER
1641	8

DATE MAILED: 12/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,120	BACUS, SARAH S.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-13 and 15-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-13 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 9/9/02 in Paper No. 7 is acknowledged and has been entered. Claims 1 and 14 have been cancelled. Claims 15-20 have been added. Accordingly, claims 2-13 and 15-20 are pending and are under examination.

Drawings

2. Applicant's submission of corrected or substitute drawings for Figures 2, 3, and 3 received on 9/9/02 is acknowledged. The drawings have been filed with the application.

Information Disclosure Statement

3. The information disclosure statement filed 9/9/02 fails to comply with 37 CFR 1.97(c) because it lacks a statement as specified in 37 CFR 1.97(e). It has been placed in the application file, but the information referred to therein has not been considered.

Rejections Moot or Withdrawn

Claim Rejections - 35 USC § 112/102

4. The rejections of claims 1-14 under 35 U.S.C. 112 and 102 are now moot in light of Applicant's cancellation of the claims.

5. In light of Applicant's amendment, the rejection of claims 2-3, 6, and 11-13 under 35 U.S.C. 102(e) as being inherently anticipated by McNamara et al. (US 6,007,996) is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2-13 and 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is vague and indefinite in relation to claim 15 from which it depends because it is unclear how the instant "immunological reagent" relate structurally and/or functionally to the "immunohistochemical stain: detectably labeled antibody" recited in claim 15.

Claim 15, step a) is vague and indefinite because it fails to distinctly define how the quantity of target protein in the first portion of control cell pellets is "determined". Specifically in step a), there is no stain or label recited to define the target protein and it does not appear to use average optical density measurements to obtain a quantity of the target protein. Please clarify.

Claim 15, step d) is vague and indefinite because it is unclear how a calibration curve is generated relating the target protein quantity obtained in a) with the average

protein density of target protein obtained in c), in the absence of how the quantity of target protein in a) is determined, i.e. units of measurement.

Regarding claim 17, the negative limitation "not embedded in paraffin" renders the claim indefinite because the claim appears to include elements/limitations not actually disclosed (those encompassed by "not ... embedded in paraffin"), thereby rendering the scope of the claim unascertainable.

Regarding claim 18, the negative limitation "not immobilized in a hydrophilic matrix" renders the claim indefinite because the claim appears to include elements/limitations not actually disclosed (those encompassed by "not ... immobilized in a hydrophilic matrix "), thereby rendering the scope of the claim unascertainable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 17-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In this case, nowhere in the specification provides literal or descriptive support for the recitation of "the calibration curve is linear" and none of the original claims recite this limitation in question. Additionally, the specification does not appear to provide any

literal support for the recitation of "control cell pellets are not embedded in paraffin" and "control cell pellets are not immobilized in hydrophilic matrix", which are negative limitations in the claims excluding other forms of immobilizing control cell pellets, i.e. embedding in paraffin, immobilizing into hydrophilic matrix. Specific guidance for such exclusion is not taught, the recitation of the negative limitation is therefore not supported or disclosed in the instant specification, these phrases do not flow from the specification, and is therefore considered to encompass new matter. See In re ANDERSON, 176 USPQ 331 (CCPA 1973).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 2-11, 13, 15-18, and 20 are rejected under 35 U.S.C. 102(b) as being inherently anticipated by Slamon et al. (US 5,846,749) for reason of record and reiterated as follows.

Slamon et al. disclose a method of determining expression level of target protein in cells from a homogeneous cell population by immunohistochemically staining the cells in order to provide a spectrophotometric signal capable of quantitation by computerized image analysis. Slamon et al. use immunohistochemically stained control cell pellets (standards) with the method to relate the spectrophotometric signal to the

quantitative amount of target protein on an individual cell basis. (See column 2, lines 17-28 and line 58, bridging to column 3, line 27). Specifically, Slamon et al. use two or more control cell pellets (cell compositions) each having different amounts of target protein. The control cells express reproducible amounts of the target protein in different levels within a desired range (see column 4, lines 14-35). All values obtained from the control cell pellets may be normalized based on the values obtained in direct comparison of the values (see column 4, lines 42-44). Slamon et al. disclose staining the cells using detectably-labeled antibodies directed against the target protein, i.e. surface membrane protein receptor, organelle protein, including glycoproteins, etc. (see column 2, lines 29-51). Various labels for immunohistochemical staining include fluorescers and enzymes which produce a product which absorbs light or fluoresces (chromagen) (see column 3, lines 34-54). In the method, Slamon et al. specifically disclose immunohistochemically assaying the sample and control cell pellets at the same time so as to obtain a direct correlation between the amount of protein present in the cells per cell and the optical density signal observed with the immunohistochemical staining. Thereafter, Slamon et al. prepare a calibration curve relating the optical signal observed with the immunohistochemical staining and the amount of target protein present in the pellet cells. Alternatively, Slamon et al. disclose using a standard curve obtained from a plurality of determinations where the curve is determined by at least two or more assay determinations. Assays used include enzyme linked immunosorbent assay (ELISA). The signal obtained from the sample is related to the concentration curve relating signal to concentration, to concentration of the target protein with known

amounts of the protein in the control cell pellets (see column 5). Slamon et al. teach application of the method in determining malignant cell expression in an animal, i.e. Her2/neu overexpression (see columns 7-8).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Slamon et al. (US 5,846,749) in view of McNamara et al. (US 6,007,996).

Slamon et al. has been discussed supra. Slamon et al. differ from the instant invention in failing to disclose staining the biological sample with multiplicity of stains upon which image analysis is performed.

McNamara et al. disclose a method of in situ analysis of biological sample by staining the sample with four different immunohistochemical stains and collecting spectral data wherein each spectrum is associated with a target protein, i.e. cytological marker, that is individually detectable. McNamara et al. use optical filters, i.e. filter-based spectral data collection device, so that each signal from each of the multiplicity of stains used to stain the sample is obtained (see column 31, lines 61-67, column 35, lines 27-38, and column 37). The immunohistochemical stain comprises detectably labeled antibodies, i.e. anti-Her-2/neu antibody (multiple cancers), which bind target

proteins, i.e. Her-2/neu, within or on the cells (see column 36, lines 34-42 and columns 40-41). Detectable labels are listed in column 38, lines 36 to column 39, line 40. McNamara et al. specifically disclose immunohistochemically staining control cells (calibration or reference material) which are simultaneously co-stained with the biological sample, obtaining optical density measurements, and comparing results therebetween (see column 38, lines 4-24).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate multiple immunohistochemical staining as taught by McNamara into the cellular samples in the method of Slamon wherein quantitative optical density measurement of target proteins is performed using image analysis because McNamara specifically taught that use of multiple immunohistochemical staining in combination with spectral imaging allows for simultaneous detection of a plurality of distinct components or target proteins present in a cell.

10. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Slamon et al. (US 5,846,749).

Slamon et al. has been discussed supra. Slamon et al. differ from the instant invention in failing to disclose that the calibration curve is linear.

However, calibration data obtained from standards used in calibration procedures all comprise result effective variables, which the prior art references have shown, are obtained using optimization procedures. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value

of a result effective variable. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitation recited in instant claim 19 is for any particular purpose or solve any stated problem and the prior art teaches that calibration curves vary according to the standards being analyzed and conditions incorporated thereto, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art to provide a linear calibration curve, by normal optimization procedures.

Response to Arguments

11. Applicant's arguments filed 9/9/02 have been fully considered but they are not persuasive.

A) Applicant argues that Slamon et al. does not anticipate the claimed invention because it fails to teach or suggest 1) a calibration curve that is generated relating the quantity of the target protein with an average optical density of target protein-specific staining and 2) a calibration curve that is generated with at least two control cell pellets that have different quantities of the target protein.

Contrary to Applicant's argument, Slamon et al. inherently anticipate the claimed invention because Slamon et al. teach obtaining two or more control cell pellets having the same or distinct target proteins at different quantities. These control cell pellets are treated in the same way as the cell pellets from a biological sample being tested (see

column 3, lines 14-18 and column 4, lines 14-24). Slamon et al. disclose determining a quantity of the target protein in a plurality of control pellets using densitometric scanning or gamma counting. Additionally, another group of control cell pellets are stained immunohistochemically using detectably labeled antibody then optical density measurements are obtained using CAS 200 computerized imaging system. At page 7, lines 9-15 of Applicant's disclosure, Applicant uses CAS 200 system as image analysis device for performing optical density measurements. According to Slamon et al., the biological samples of interest are examined in conjunction with the control cell pellets upon which a standard calibration curve is prepared and used with subsequent determinations of the biological samples (see column 5, lines 3-67).

Accordingly, claims 2-11, 13, 15-18, and 20 are deemed to be anticipated by Slamon et al.

12. For reasons aforementioned, no claims are allowed.

13. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday 6:00 AM to 3:30 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641

Gailene R. Gabel
December 10, 2002